REMARKS

This is in response to the Office Action that was mailed on November 5, 2002. The specification has been amended to recite the U.S. patent number corresponding to application Serial No. 08/596,405. Inasmuch as there appears to be a discrepancy between the claims in the Examiner's file and the claims in Applicants' file, all of the claims acknowledged by the Examiner to be pending are cancelled. New claims 30-54 correspond approximately to claims 1-6, 26, 7-13, 15-17, 32, and 27-31 in Applicants' file. Independent claims 30, 37, and 49 differ from former claims 1, 26, and 29, however, in their more precise definition of variants of SEQ ID NO:10. The more precise definition is based upon disclosure appearing in lines 12-31 on page 23 of the specification. New claims 31, 38, and 50 are based upon disclosure in lines 12-17 on page 23 of the specification. No new matter is introduced by this Amendment. Claims 30-54 are pending in the application.

Regarding the requirement for restriction that was set forth in the Office Action of November 22, 2000, the Examiner is respectfully requested to withdraw that requirement to the extent that it divides out any of the claims remaining in this application. Alternatively, the Examiner is requested to restate the requirement for restriction with respect to the claims now before her.

The Examiner is correct in noting that the claim for priority that was filed on October 26, 1999 is a claim under 35 U.S.C. §119(e) to the benefit of U.S. provisional application Serial No. 60/106,426.

Claims 1-6 and 15-17 were rejected as allegedly failing to satisfy the written description requirement of the first paragraph of 35 U.S.C. §112. This ground of rejection is clearly not applicable to the claims presently in

the application because independent claims 30, 37, and 49 all recite a precise definition of variants of SEQ ID NO:10 that is based upon disclosure appearing in lines 12-31 on page 23 of the specification. New subgeneric claims 31, 38, and 50 are based upon disclosure in lines 12-17 on page 23 of the specification. The remaining claims, all of which are narrower in scope than claims 30, 37, and 49, correspond to originally presented dependent claims. The specification therefore contains a written description of the invention that is presently claimed.

Claim 17 was rejected as failing to define the invention properly, as required by the second paragraph of 35 U.S.C. §112. The Examiner indicated that the acronyms COS, CHO, and EPC should be spelled out. Claim 47 spells out the terminology represented by the acronyms CHO and EPC. However, COS cells are an established monkey kidney cell line well recognized in the art. It is respectfully submitted that the claims in their present form satisfy the requirements of the statute.

Claim 1 was rejected under U.S.C. §102(b) as being anticipated by La Fleur. The Examiner alleges that the La Fleur amino acid sequence directs secretion and cleavage of the secretory signal as required by the present claim and that, due to the use of the term "comprising" the whole of the *F. heteroclitus* vitellogenin cDNA is within the scope of the present claims. Applicants disagree, for instance because the sequence recited in the present claims is the *O. aureus* secretory sequence having a diffferent overall amino acid sequence. In any case, all of the claims herein now stipulate that the G and D residues constituting the cleavage site are retained or that D is replaced by E and/or G is replaced by A or V; this still further distinguishes the present invention from the disclosure of La Fleur.

Claim 1 was rejected under U.S.C. §102(b) as being anticipated by the

Lim citation (which is reflective of Applicants' own prior work). Applicants respectfully traverse this rejection. The sequence of the Lim citation is not seen to describe directing secretion of a fusion protein from a cell and cleavage of the secretory signal sequence from the fusion protein in the manner contemplated by claim 30. Lim is entirely devoid of any suggestion of joining the secretory sequence in question to a heterologous protein as required by claim 36 or to a heterologous polypeptide as in claim 47.

In any case, the Lim citation is not competent as a reference against the present application. AF017250 (nucleotide sequence) and AAD01615 (amino acid sequence) were submitted to NCBI genbank on 5 August 1997, *but were not released until 5 January 1999.* Note that the reference itself contains the notation "unpublished", and also a "VRT" date of January 5, 1999. The presently claimed invention, however, is entitled under 35 U.S.C. §119(e) to the benefit of provisional application 60/106,426, filed 30 October 1998, well before publication of the Lim citation.

Claims 3 and 4 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lim in view of Lee (which latter reference also reflects Applicants' own prior work). ***The Lim reference fails for reasons discussed above.*** Lee alone is not sufficient to describe or suggest the present invention. Lee's Vtg cDNA clones were only 3'-end partial fragments of the very long Vtg cDNA, and therefore there was no 5'-end region of Vtg in the Lee clones. Hence, the partial Vtg clones disclosed by Lee do not harbor any secretory sequence, much less disclose their expression in prokaryotic or eukaryotic cells. On page 75, last paragraph, 2nd and 3rd lines, Lee states that "Estradiol-induced Vg gene expression in *O. aureus* has been documented (17, 18)." This statement refers to *in vivo* experiments the previous authors carried out to induce Vg gene expression by injecting estradiol into fish and merely shows that the Vg gene of *O. aureus* is steroid

inducible. It does not refer any secretory sequence of any Vtg gene.

Claims 15-17 were rejected under U.S.C. §103(a) as being unpatentable over Lim in view of Yarranton. ***The primary reference, Lim, fails for reasons discussed above.*** Yarranton alone does not describe or suggest the present invention. Yarranton's paper is a general review on gene expression in prokaryotes and eukaryotes, but fails to specify details of any secretory signals, or to show evidence of how those signals work.

Favorable action on the merits of all of the claims remaining in the application is respectfully requested. If there be minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Mr. Richard Gallagher, (Reg. No. 28,781) at (703) 205-8008.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,
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Marked up text showing changes:

IN THE SPECIFICATION:

The paragraph bridging pages 26-27 of the specification is amended as follows:

In other embodiments of the invention, it is desirable to produce a lipopolysaccharide-binding protein, such as Factor C of a horseshoe crab. Cloned cDNAs encoding Factor C from at least two species of horseshoe crab are known (*see,* U.S. Patent 5,716,834 and Muta et al., *J. Biol. Chem.* 266:6554-6561 (1991)). The lipopolysaccharide-binding protein produced by the present invention can be used in the ways described in U.S. Patents 5,712,144, 5,716,834, and 5,858,706 [and 5,716,834 and in co-pending applications 08/596,405 and 09/081,767]. In those embodiments of the invention directed to production of a protein for quantitative assay or purification, it is most desired that cells that do not secrete proteases are used. Preferred host cells are COS, CHO, NIH/3T3, *Drosophila* cells, especially Schneider 2 cells, piscine epithelial cells (EPC) and yeast cells, such as *S. cerevisiae* and *S. pombe* and *Pichia* spp., especially protease-deficient yeast cells.

IN THE CLAIMS:

Claims 1-9, 11-13, 15-17 and 26-29 have been canceled.

Claims 30-54 have been added.